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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,634	04/29/2005	Bruce Ivins	4239-67021-06	5041

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KLARQUIST SPARKMAN, LLP
121 S.W. SALMON STREET
SUITE #1600
PORTLAND, OR 97204-2988

EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,634	IVINS ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/29/05, 11/09/07, 12/18/07+ 05/07/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-15,18,19,37,38,40,41,50,52-57 and 61-64* is/are pending in the application.

4a) Of the above claim(s) *1-4,6-15,18,19 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37,38,40,41,50,52-57 and 61-64* is/are rejected.

7)☒ Claim(s) *64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/24/06, 03/06/07+05/07/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II in the reply filed on 11/09/2007 is acknowledged. The traversal is on the ground(s) that there would not be an undue burden on the Examiner to examine the claims of Groups I and II together because the present application is directed at immunostimulatory oligonucleotides that can be used to induce an immune response that can be used to treat an infection. This is not found persuasive.

As noted in the restriction requirement, serious search and examination burden if restriction were not required can be established by one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

In the instant case, items (d) and (e) are most applicable. The search for the use of immunostimulatory oligonucleotide as an adjuvant in vaccine compositions is different from the search for the use of such oligonucleotide as the active ingredient in treating infection. A prior art found for the use of the oligonucleotide as an adjuvant would not be applicable for the use of the oligonucleotide as a treating composition against infections. Additionally, the inventions of Group I and II raise different non-prior art issues under 35 U.S.C. 112, first paragraph, the enablement requirement. In the instant case, the enablement evaluation for each of the listed inventions is different from one another. The enablement evaluation of the invention of Group I is more extensive than the enablement evaluation for the invention of Group II. In the instant case, because of the reason(s) provided above, serious search burden would be imposed on the Office for the examination of more than one invention.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election without traverse of species SEQ ID NO: 200 and *Bacillus anthracis* in the reply filed on 11/09/2007 is acknowledged.

Status of Claims

2. Claims 61-64 are added. Claims 5, 16-17, 20-36, 39, 42-49, 51 and 58-60 are cancelled. Claims 1-4, 6-15, 18-19, 37-38, 40-41, 50, 52-57 and 61-64 are pending. Claims 1-4, 6-15, 18-19 and 50 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/09/2007. Claims 37-38, 40-41, 52-57 and 61-64 are under

examination. It is noted that Applicant submits that claims 37-38, 40-42, 52-57 and 61-64 are directed to the elected invention and species. However, it is found that claim 42 is cancelled. Therefore, claim 42 cannot read on the elected species.

Claim Objections

3. Claim 63 is objected to because of the following informalities: the recitation "comprises and increase" should be "comprises an increase". Appropriate correction is required.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 37-38, 40-41, 50, 52-57 and 61-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ivins et al.[1] in view of Verthelyi et al.[2] and Jones et al.[3]

The claims are directed at to a process of enhancing the immunogenicity of a vaccine comprising administering an anthrax antigen or vaccine and a CpG containing oligonucleotide having the sequence set forth in SEQ IDNO: 200 to a subject. Claim 38, which depends on claim 37, requires the vaccine to be an antigen vaccine, a DNA vaccine, a protein subunit vaccine, a peptide vaccine, an attenuated vaccine or a heat-

[1] Ivins et al. Recent advances in the development of an improved, human anthrax vaccine. Eur. J. Epidemiol., March 1988, Vol. 4, No. 1, p. 12-19.
[2] Verthelyi et al. CpG oligodeoxynucleotides as vaccine adjuvants in primates. The Journal of Immunology, February 15, 2002, Vol. 168, 1659-1663.

killed vaccine. Claim 40, which depends on claim 37, requires the antigen be from *Bacillus anthracis*. Claim 41, which depends on claim 40, requires the antigen to be a recombinant protective antigen or protective antigen. Claim 52, which depends on claim 37, requires that the oligonucleotide is administered before the vaccine is administered to the subject. Claim 53, which depends on claim 52, requires that the oligonucleotide is administered about two weeks to about one day before the vaccine is administered. Claim 54, which depends on claim 37, requires that oligonucleotide is administered concurrently with the vaccine. Claim 55, which depends on claim 37, requires that the oligonucleotide is administered after the vaccine is administered to the subject. Claim 56, which depends on claim 55, requires that the oligonucleotide is administered from about two weeks to about one day after the vaccine is administered to the subject. Claim 64, which depends on claim 37, requires the vaccine be Anthrax Vaccine Adsorbed (AVA). Claim 57 is directed to the process of claim 64. Claim 62, which depends on claim 57, requires that the administration enhances the immunogenicity of AVA by increasing IgG or IgM titer. Claim 63, which depends on claim 57, requires that the administration enhances the immunogenicity of AVA by increasing the survival of the subject upon subsequent exposure to anthrax. Claim 61 is directed at the invention of claim 41.

Ivins et al. teaches the Anthrax Vaccine Adsorbed (AVA) vaccine, which is an anthrax vaccine comprising protective antigen, which is an antigen from *Bacillus anthracis*. [Abstract, in particular.]

[3] Jones et al. Synthetic oligodeoxynucleotides containing CpG motifs enhance immunogenicity of a

Ivins et al. does not teach the use of CpG oligonucleotides as an adjuvant to the vaccine. However, at the time the invention was made, it is noted that the immunity elicited by alum or aluminum hydroxide appears to be suboptimal, and suggests the use other adjuvants that may potentate immunity to anthrax. [Last paragraph, left column, page 17, in particular.]

At the time the invention was made, Verthelyi et al. establishes the use of CpG oligonucleotides as vaccine adjuvants in primates. [Title and Abstract, in particular.] Verthelyi et al. teaches that the oligonucleotides boost humoral and cellular responses, including IgG titers. Verthelyi et al. does not teach a CpG oligonucleotide having the sequence set forth in SEQ ID NO: 200, however, Jones et al. teaches an oligonucleotide having the same sequence as SEQ ID NO: 200. [Section 2, Materials and Methods, page 3066, see ODN 2006, in particular.]

Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to use the adjuvant of Jones et al. with the vaccine of Ivins et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to potentiate the immunity of the anthrax vaccine of Ivins et al. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the use of CpG oligonucleotides as adjuvants in primates have been demonstrated by Verthelyi et al.

Regarding the limitations of claims 52-56, which are directed to various administration protocols between the vaccine and the oligonucleotide. In the instant

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peptide malaria vaccine in Aotus monkeys. Vaccine, 1999, Vol. 17, 3065-3071.

case, it would have been prima facie obvious for one of ordinary skill in the art to vary the administration protocols between the vaccine and the oligonucleotide. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to optimize enhance of immunogenicity of anthrax by modifying the administration protocol. One of ordinary skill in the art, at the time the invention as made, would have had a reasonable expectation of success for doing so because the determination of a workable or optimal range and administration protocols are routinely practiced in the art.

Regarding the limitation of claim 63, which requires that the administration of the vaccine and oligonucleotide to increase the survival of the subject upon exposure to anthrax, it the instant case, such protection would inherently be provided to the subject receiving the anthrax vaccine for the essence of a vaccine is to protect a subject from exposure, including subsequent exposure.

Conclusion

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Emily Le/
Primary Examiner, Art Unit 1648

/E. L./